Practitioner's Docket No. U 015859-4

## Optional Customer No. Bar Code

00140

PATENT TRADEMARK OFFICE

CHAPTER II

## TRANSMITTAL LETTER
## TO THE UNITED STATES ELECTED OFFICE (EO/US)
## (ENTRY INTO U.S. NATIONAL PHASE UNDER CHAPTER II)

| INTERNATIONAL APPLICATION NO. | INTERNATIONAL FILING DATE | PRIORITY DATE CLAIMED |
|---|---|---|
| PCT/ES2004/070001 | 21 JANUARY 2004 | 28 JANUARY 2003, etc. |

TITLE OF INVENTION
METHOD AND DEVICE FOR THE DETECTION OF MUTATIONS IN ISOLATED GENE SEQUENCES OF THE LOW-DENSITY LIPOPROTEIN RECEPTOR (LDL-R) WHICH IS ASSOCIATED WITH FAMILIAL HYPERCHOLESTEROLEMIA

APPLICANT(S)

| | | |
|---|---|---|
| 1. | MATA LOPEZ, PEDRO |
| 2. | LONSO KARLEZI, RODRIGO, ALBERTO |
| 3. | MOZAS ALONSO, PILAR |
| 4. | REYES LEAL, GILBERTO |
| 5. | POCOVI MIERAS, MIGUEL |
| 6. | CASTILLO FERNANDEZ, SERGIO |
| 7. | TEJEDOR HERNANDEZ, DIEGO |
| 8. | MARTINEZ MARTINEZ, ANTONIO |
| 9. | MALLEN PEREZ, MIGUEL |

Mail Stop PCT
Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

Date of this paper: December 11, 2009

## SUBMISSION OF "SEQUENCE LISTING," COMPUTER READABLE COPY,
## AND/OR AMENDMENT PERTAINING THERETO
## FOR BIOTECHNOLOGY INVENTION CONTAINING NUCLEOTIDE
## AND/OR AMINO ACID SEQUENCE

*(check and complete this item, if applicable)*

1. [✓]This replies to the Office Letter dated <u>June 24, 2009</u>

*NOTE:* *If these papers are filed before the office letter issues, adequate identification of the original papers should be made, e.g., in addition to the name of the inventor and title of invention, the filing date based on the "Express Mail" procedure, the serial number from the return post card or the attorney's docket number added.*

[✓]A copy of the Office Letter is enclosed.

## IDENTIFICATION OF PERSON MAKING STATEMENT

2. I, <u>Janet I. Cord</u>

*(type or print name of person signing below)*

state the following:

## ITEMS BEING SUBMITTED

3. Submitted herewith is/are

*(check each item as applicable)*

A. [✓]"Sequence Listing(s)" for the nucleotide and/or amino acid sequence(s) in this application. Each "Sequence Listing" is assigned a separate identifier as required in 37 C.F.R. 1.821(c) and 37 C.F.R. 1.822 and 1.823.

B. [✓]An amendment to the description and/or claims, wherein reference is made to the sequence by use of the assigned identifier, as required in 37 C.F.R. 1.821(d).

C. [ ] A copy of each "Sequence Listing" submitted for this application in computer readable form, in accordance with the requirements of 37 C.F.R. 1.821(e) and 1.824.

D. [ ] Please transfer to this application, in accordance with 37 C.F.R. 1.821(e), the computer readable copy(ies) from applicant's other application identified as follows:

In re application of:
Serial No.:
Filed:
For:

Group No.:
Examiner:

The Computer readable form(s) of applicant's other application corresponds or compares to the "Sequence Identifier(s)" of this application as follows:

Computer Readable Form
(other applications)

"Sequence Identifier"
(this application)

NOTE: *"If the computer readable form of a new application is to be identical with the computer readable form of another application of the applicant on file in the Office, reference may be made to the other application and computer readable form in lieu of filing a duplicate computer readable form in the new application. The new application shall be accompanied by a letter making such reference to the other application and computer readable form, both of which shall be completely identified." 37 C.F.R. 1.821(e).*

E.  [ ]  A statement that the content of each "Sequence Listing" submitted and each computer readable copy are the same, as required in 37 C.F.R. 1.821(f).

   [ ]  Because the statement is not made by a person registered to practice before the Office, the Statement is verified as required in 37 C.F.R. 1.821(b).

F.  [✓]Because this submission is made in fulfilling the requirement under 37 C.F.R. 1.821(g), a statement that the submission includes no new matter.

   [ ]  Because the statement is not made by a person registered to practice before the Office, the statement is verified, as required in 37 C.F.R. 1.821(g).


## STATEMENT THAT "SEQUENCE LISTING" AND COMPUTER READABLE COPY ARE THE SAME AND/OR THAT PAPERS SUBMITTED INCLUDES NO NEW MATTER

4.  I hereby state:

*(complete applicable item A and/or B)*

A.  [ ]  Each computer readable form submitted in this application, including those forms requested to be transferred from applicant's other application, is the same as the "Sequence Listing" to which it is indicated to relate.

B.  [✓]All papers accompanying this submission, or for which a request for transfer from applicants' other application, introduce no new matter.

# STATUS

5. Applicant is

[✓] a small entity:
[ ] other than a small entity.

## EXTENSION OF TERM

6.

NOTE: 37 C.F.R. § 1.704(b)". . . an applicant shall be deemed to have failed to engage in reasonable efforts to conclude processing or examination of an application for the cumulative total of any periods of time in excess of three months that are taken to reply to any notice or action by the Office making any rejection, objection, argument, or other request, measuring such three-month period from the date the notice or action was mailed or given to the applicant, in which case the period of adjustment set forth in § 1.703 shall be reduced by the number of days, if any, beginning on the day after the date that is three months after the date of mailing or transmission of the Office communication notifying the applicant of the rejection, objection, argument, or other request and ending on the date the reply was filed. The period, or shortened statutory period, for reply that is set in the Office action or notice has no effect on the three-month period set forth in this paragraph."

NOTE: "Extension of Time in Patent Cases (Supplement Amendments) If a timely and complete response has been filed after a Non-Final Office Action, an extension of time is not required to permit filing and/or entry of an additional amendment after expiration of the shortened statutory period.

If a timely response has been filed after a Final Office Action, an extension of time is required to permit filing and/or entry of a Notice of Appeal or filing and/or entry of an additional amendment after expiration of the shortened statutory period unless the timely-filed response placed the application in condition for allowance. Of course, if a Notice of Appeal has been filed within the shortened statutory period, the period has ceased to run." Notice of Dec.10, 1985 (1061 O.G. 34-35).

NOTE: See 37 C.F.R. 1.645 for extensions of time in interference proceedings and 37 C.F.R. 1.550(c) for extensions of time in reexamination proceedings.

7. The proceedings herein are for a patent application and the provisions of 37 C.F.R. 1.136 apply.

*(complete (a) or (b) as applicable)*

(a) [✓] Applicant petitions for an extension of time under 37 C.F.R. 1.136 (fees: 37 C.F.R. 1.17(a)(1)-(4)) for the total number of months checked below:

| | Extension (months) | Fee for other than small entity | Fee for small entity |
|---|---|---|---|
| ☐ | one month | $ 130.00 | $ 65.00 |
| ☐ | two months | $ 490.00 | $ 245.00 |
| ☐ | three months | $ 1,110.00 | $ 555.00 |
| ☐ | four months | $ 1,730.00 | $ 865.00 |
| ☒ | five months | $ 2,350.00 | $ 1,175.00 |

Fee     $ 1,175.00

If an additional extension of time is required, please consider this a petition therefor.

*(check and complete the next item, if applicable)*

[ ] An extension for _____ months has already been secured, and the fee paid therefor of $ _____ is deducted from the total fee due for the total months of extension now requested.

Extension fee due with this request $ _____

## OR

(b) [ ] Applicant believes that no extension of term is required. However, this conditional petition is being made to provide for the possibility that applicant has inadvertently overlooked the need for a petition and fee for extension of time.

## FEE PAYMENT

8. [ ] Attached is a check in the sum of $                                   .

[✓] Charge Account No. 12-0425 the sum of $ 1,175.00                            .

## FEE DEFICIENCY

9.

*NOTE: If there is a fee deficiency and there is no authorization to charge an account, additional fees are necessary to cover the additional time consumed in making up the original deficiency. If the maximum, six-month period has expired before the deficiency is noted and corrected, the application is held abandoned. In those instances where authorization to charge is included, processing delays are encountered in returning the papers to the PTO finance Branch in order to apply these charges prior to action on the cases. Authorization to charge the deposit account for any fee deficiency should be checked. See the Notice of April 7, 1986, 1065 O.G. 31-33.*

10. [✓] If any additional extension and/or fee is required, charge Account No. 12-0425.

# SIGNATURE(s)

*(type or print name of person signing statement)*

**Signature**

Date

P.O. Address of Signatory

*(If applicable)*

Tel. No.: (   )
Reg. No.

[ ] Inventor
[ ] Assignee of complete interest
[ ] Person authorized to sign on behalf of assignee
[ ] Practitioner of record
[ ] Filed under Rule 34(a)
[ ] Registration No._____
[ ] Other _____

*(specify identity of person signing)*

*(complete the following, if applicable)*

PROGENIKA BIOPHARMA, S.A._____
*(type name of assignee)*

PARQUE TECNOLOGICO DE BIZKAIA
EDIFICIO 801B
48160 DERIO, VIZCAYA, SPAIN_____
Address of assignee

Title of person authorized to sign on behalf of assignee

A "STATEMENT UNDER 37 C.F.R. 3.73(b)" is attached.

Assignment recorded in PTO on **JANUARY 16, 2008**
**Reel 020390  Frame 0770**

Reg. No.: 33,778

Tel. No.: (212)708-1935

Customer No.: 00140.

**00140**
PATENT TRADEMARK OFFICE

**SIGNATURE OF PRACTITIONER**
Janet  I.  Cord

*(type or print name of practitioner)*

P.O. Address

c/o Ladas & Parry LLP
26 West 61st Street
New York, N.Y. 10023

# UNITED STATES PATENT AND TRADEMARK OFFICE

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/542,937 | 09/08/2006 | Pedro Mata Lopez | U 015859-4 | 5381 |

140        7590        06/24/2009
LADAS & PARRY LLP
26 WEST 61ST STREET
NEW YORK, NY 10023

| EXAMINER |
|---|
| KAPUSHOC, STEPHEN THOMAS |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1634 | |

| MAIL DATE | DELIVERY MODE |
|---|---|
| 06/24/2009 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

PTOL-90A (Rev. 04/07)

## *Non-Responsive Amendment of the Application*

1.      The reply filed on 04/13/2009 is not fully responsive to the prior Office Action

because of the following omission(s) or matter(s): The Office Action of 01/06/2009 set

forth an objection to the specification for failure to comply with the Sequence Rules (see

p.3 of the Office Action of 01/06/2009).  In Response to the previous Office Action it

appears that Applicants have submitted a new Sequence Listing, however the newly

submitted Sequence Listing of 04/13/2009 is defective.  Please see the attached copy

of the CRFD and validation report of 04/25/2009 associated with the submitted

Sequence Listing.  As such the attempted amendments to the specification are not fully

responsive to the objection as set forth in the previous Office Action.  See 37 CFR

1.111.

2.      Since the above-mentioned reply appears to be *bona fide*, a time period for reply

is set forth on the PTO-90C included with this mailing.


/Stephen  Kapushoc/
Examiner, Art Unit 1634

* * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *

Reviewer Comments:
<120> Device a method for detecting low density lipoprotein receptor
gene mutations associated with familial hypercholesterolemia

The above <120> response exceeds the Sequence Rules' required 72-
character line limit; please adjust the line.


<210> SEQ 1

Please remove the "SEQ" in the above <210> response; just show <210> 1.
This error appears in subsequent sequences.

(from Sequence 1)
atatggtatt tattatgcac cgagtgtggc tctaatcact tttttttttt taattgagag 10920
acagcctggc tctgttgatt gggctggagt gcagtggcgc gaccgtagct cattgcagcc 10980


Please show only one space between groups of nucleotides.

actgcctggc agaggctgcg agc atg ggg ccc tgg ggc tgg aaa ttg cgc  15350
        met gly pro trp gly trp lys leu arg
     -21 -20              -15
tgg acc gtc gcc ttg ctc ctc gcc gcg gcg ggg act gca g gtaaggcttg 15400
trp thr val ala leu leu leu ala ala ala gly thr ala v
        -10              -5            -1  1


Please show the initial letters of the above amino acids in upper-case
letters (e.g., Met Gly). Please show all codons as three letters with a
space between each codon.

```
<210> SEQ 2
<211> 24
<212> DNA
<213> Artificial   sequence
<220>
<221> oligonucleotide
<223> Ex1F
```

Remove "SEQ" from the above <210> line; also, move "oligonucleotide" to the <223> line.  Same error in subsequent sequences.

\* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \*

Application No:     10542937          Version No:        2.0

Input Set:

Output Set:

Started:     2009-04-15 14:29:52.963
Finished:    2009-04-15 14:30:12.857
Elapsed:     0 hr(s) 0 min(s) 19 sec(s) 894 ms
Total Warnings:    341
Total Errors:    2028
No. of SeqIDs Defined:    259
Actual SeqID Count:    238

| Error code | Error Description |
|---|---|
| E  202 | Invalid input format; Value must be an integerin <210> in SEQID |
| W  402 | Undefined organism found in <213>  in SEQ ID (0) |
| E  259 | Found undefined lettercode; POS (281) SEQID(0) |
| E  254 | The total number of bases conflicts with running total, Input: 300,  Calculated : 301 SEQID(0) |
| E  254 | The total number of bases conflicts with running total, Input: 360,  Calculated : 361 SEQID(0) |
| E  254 | The total number of bases conflicts with running total, Input: 420,  Calculated : 421 SEQID(0) |
| E  254 | The total number of bases conflicts with running total, Input: 480,  Calculated : 481 SEQID(0) |
| E  254 | The total number of bases conflicts with running total, Input: 540,  Calculated : 541 SEQID(0) |
| E  254 | The total number of bases conflicts with running total, Input: 600,  Calculated : 601 SEQID(0) |
| E  254 | The total number of bases conflicts with running total, Input: 660,  Calculated : 661 SEQID(0) |
| E  254 | The total number of bases conflicts with running total, Input: 720,  Calculated : 721 SEQID(0) |
| E  254 | The total number of bases conflicts with running total, Input: 780,  Calculated : 781 SEQID(0) |
| E  254 | The total number of bases conflicts with running total, Input: 840,  Calculated : 841 SEQID(0) |
| E  254 | The total number of bases conflicts with running total, Input: 900,  Calculated : 901 SEQID(0) |
| E  254 | The total number of bases conflicts with running total, Input: |

```
            Input Set:


            Output Set:



                 Started:  2009-04-15 14:29:52.963
                Finished:  2009-04-15 14:30:12.857
                 Elapsed:  0 hr(s) 0 min(s) 19 sec(s) 894 ms
          Total Warnings:  341
            Total Errors:  2028
    No. of SeqIDs Defined:  259
        Actual SeqID Count:  238


Error code       Error Description

                 961 SEQID(0)

E   254          The total number of bases conflicts with running total, Input:
                 1020,  Calculated : 1021 SEQID(0)

E   254          The total number of bases conflicts with running total, Input:
                 1080,  Calculated : 1081 SEQID(0)

E   254          The total number of bases conflicts with running total, Input:
                 1140,  Calculated : 1141 SEQID(0)

E   254          The total number of bases conflicts with running total, Input:
                 1200,  Calculated : 1201 SEQID(0)

E   254          The total number of bases conflicts with running total, Input:
                 1260,  Calculated : 1261 SEQID(0)

E   254          The total number of bases conflicts with running total, Input:
                 1320,  Calculated : 1321 SEQID(0)

E   254          The total number of bases conflicts with running total, Input:
                 1380,  Calculated : 1381 SEQID(0)

E   254          The total number of bases conflicts with running total, Input:
                 1440,  Calculated : 1441 SEQID(0)
                 This error has occured more than 20 times, will not be displayed

E   259          Found undefined lettercode; POS (8762) SEQID(0)

E   259          Found undefined lettercode; POS (8773) SEQID(0)

E   259          Found undefined lettercode; POS (8794) SEQID(0)

E   259          Found undefined lettercode; POS (8805) SEQID(0)

E   259          Found undefined lettercode; POS (8816) SEQID(0)

E   259          Found undefined lettercode; POS (8827) SEQID(0)

E   259          Found undefined lettercode; POS (8838) SEQID(0)

E   259          Found undefined lettercode; POS (8849) SEQID(0)

E   259          Found undefined lettercode; POS (8860) SEQID(0)
```

Input Set:


Output Set:


| | |
|---|---|
| **Started:** | 2009-04-15 14:29:52.963 |
| **Finished:** | 2009-04-15 14:30:12.857 |
| **Elapsed:** | 0 hr(s) 0 min(s) 19 sec(s) 894 ms |
| **Total Warnings:** | 341 |
| **Total Errors:** | 2028 |
| **No. of SeqIDs Defined:** | 259 |
| **Actual SeqID Count:** | 238 |

| Error code | | Error Description |
|---|---|---|
| E | 259 | Found undefined lettercode; POS (8871) SEQID(0) |
| W | 333 | tabs used in amino acid numbering   SEQID (0) |
| W | 333 | tabs used in amino acid numbering   SEQID (0) |
| W | 333 | tabs used in amino acid numbering   SEQID (0) |
| E | 342 | 'n' position not defined  found at POS:   26149 SEQID(0) |
| E | 342 | 'n' position not defined  found at POS:   26158 SEQID(0) |
| E | 342 | 'n' position not defined  found at POS:   26164 SEQID(0) |
| W | 333 | tabs used in amino acid numbering   SEQID (0) |
| E | 342 | 'n' position not defined  found at POS:   26266 SEQID(0) |
| E | 342 | 'n' position not defined  found at POS:   26287 SEQID(0) |
| W | 333 | tabs used in amino acid numbering   SEQID (0) |
| E | 323 | Invalid/missing amino acid numbering  SEQID (0)   POS (1) |
| E | 342 | 'n' position not defined  found at POS:   28723 SEQID(0) |
| W | 333 | tabs used in amino acid numbering   SEQID (0) |
| E | 342 | 'n' position not defined  found at POS:   28786 SEQID(0) |
| E | 342 | 'n' position not defined  found at POS:   28807 SEQID(0) |
| W | 333 | tabs used in amino acid numbering   SEQID (0) |
| E | 342 | 'n' position not defined  found at POS:   28867 SEQID(0) |
| E | 342 | 'n' position not defined  found at POS:   28882 SEQID(0) |
| W | 333 | tabs used in amino acid numbering   SEQID (0) |
| E | 342 | 'n' position not defined  found at POS:   31357 SEQID(0) |
| W | 333 | tabs used in amino acid numbering  SEQID (0) |

```
              Input Set:


              Output Set:



              Started:   2009-04-15 14:29:52.963
             Finished:   2009-04-15 14:30:12.857
              Elapsed:   0 hr(s) 0 min(s) 19 sec(s) 894 ms
      Total Warnings:    341
        Total Errors:    2028
  No. of SeqIDs Defined: 259
    Actual SeqID Count:  238
```

| Error code | Error Description |
|---|---|
| E 342 | 'n' position not defined found at POS: 31443 SEQID(0) |
| W 333 | tabs used in amino acid numbering SEQID (0) |
| E 323 | Invalid/missing amino acid numbering SEQID (0) POS (4) |
| E 323 | Invalid/missing amino acid numbering SEQID (0)at Protein (5) |
| E 323 | Invalid/missing amino acid numbering SEQID (0) POS (9) |
| E 323 | Invalid/missing amino acid numbering SEQID (0)at Protein (10) |
| E 323 | Invalid/missing amino acid numbering SEQID (0) POS (14) |
| E 323 | Invalid/missing amino acid numbering SEQID (0)at Protein (15) |
| E 342 | 'n' position not defined found at POS: 31626 SEQID(0) |
| E 342 | 'n' position not defined found at POS: 31632 SEQID(0) |
| E 342 | 'n' position not defined found at POS: 31653 SEQID(0) |
| E 323 | Invalid/missing amino acid numbering SEQID (0) POS (3) |
| E 323 | Invalid/missing amino acid numbering SEQID (0)at Protein (5) |
| E 323 | Invalid/missing amino acid numbering SEQID (0) POS (8) |
| E 323 | Invalid/missing amino acid numbering SEQID (0)at Protein (10) |
| E 323 | Invalid/missing amino acid numbering SEQID (0) POS (13) |
| E 323 | Invalid/missing amino acid numbering SEQID (0)at Protein (15) |
| E 342 | 'n' position not defined found at POS: 31719 SEQID(0) |
| E 323 | Invalid/missing amino acid numbering SEQID (0) POS (2) |
| E 323 | Invalid/missing amino acid numbering SEQID (0)at Protein (5) |
| E 323 | Invalid/missing amino acid numbering SEQID (0) POS (7) |
| E 323 | Invalid/missing amino acid numbering SEQID (0)at Protein (10) |

```
          Input Set:


          Output Set:



                   Started:   2009-04-15 14:29:52.963
                  Finished:   2009-04-15 14:30:12.857
                   Elapsed:   0 hr(s) 0 min(s) 19 sec(s) 894 ms
           Total Warnings:    341
             Total Errors:    2028
   No. of SeqIDs Defined:     259
       Actual SeqID Count:    238
```

| Error code | Error Description |
|---|---|
| E 323 | Invalid/missing amino acid numbering  SEQID (0)  POS (12) |
| E 323 | Invalid/missing amino acid numbering SEQID (0) at Protein (15) |
| E 342 | 'n' position not defined  found at POS:  31806 SEQID(0) |
| E 342 | 'n' position not defined  found at POS:  31833 SEQID(0) |
| E 323 | Invalid/missing amino acid numbering  SEQID (0)  POS (1)<br> This error has occured more than 20 times, will not be displayed |
| E 342 | 'n' position not defined  found at POS:  32096 SEQID(0) |
| E 342 | 'n' position not defined  found at POS:  33124 SEQID(0)<br> This error has occured more than 20 times, will not be displayed |
| W 333 | tabs used in amino acid numbering  SEQID (0) |
| W 333 | tabs used in amino acid numbering  SEQID (0) |
| W 333 | tabs used in amino acid numbering  SEQID (0) |
| W 333 | tabs used in amino acid numbering  SEQID (0) |
| W 333 | tabs used in amino acid numbering  SEQID (0) |
| W 333 | tabs used in amino acid numbering  SEQID (0) |
| W 333 | tabs used in amino acid numbering  SEQID (0) |
| W 333 | tabs used in amino acid numbering  SEQID (0) |
| W 333 | tabs used in amino acid numbering  SEQID (0) |
| E 253 | The number of bases differs from <211>  Input: 60000<br>Calculated:62488 SEQID (0) |
| E 202 | Invalid input format; Value must be an integerin <210> in SEQID |
| W 402 | Undefined organism found in <213>  in SEQ ID (0) |
| E 257 | Invalid sequence data feature in <221>  in SEQ ID (0) |
| E 202 | Invalid input format; Value must be an integerin <210> in SEQID |

```
               Input Set:


               Output Set:



            Started:   2009-04-15 14:29:52.963
           Finished:   2009-04-15 14:30:12.857
            Elapsed:   0 hr(s) 0 min(s) 19 sec(s) 894 ms
     Total Warnings:   341
       Total Errors:   2028
No. of SeqIDs Defined:   259
   Actual SeqID Count:   238
```

| Error code | | Error Description |
|---|---|---|
| W | 402 | Undefined organism found in \<213\>  in SEQ ID (0) |
| E | 257 | Invalid sequence data feature in \<221\>  in SEQ ID (0) |
| E | 202 | Invalid input format; Value must be an integerin \<210\> in SEQID |
| W | 402 | Undefined organism found in \<213\>  in SEQ ID (0) |
| E | 257 | Invalid sequence data feature in \<221\>  in SEQ ID (0) |
| E | 202 | Invalid input format; Value must be an integerin \<210\> in SEQID |
| W | 402 | Undefined organism found in \<213\>  in SEQ ID (0) |
| E | 257 | Invalid sequence data feature in \<221\>  in SEQ ID (0) |
| E | 202 | Invalid input format; Value must be an integerin \<210\> in SEQID |
| W | 402 | Undefined organism found in \<213\>  in SEQ ID (0) |
| E | 257 | Invalid sequence data feature in \<221\>  in SEQ ID (0) |
| E | 202 | Invalid input format; Value must be an integerin \<210\> in SEQID |
| W | 402 | Undefined organism found in \<213\>  in SEQ ID (0) |
| E | 257 | Invalid sequence data feature in \<221\>  in SEQ ID (0) |
| E | 202 | Invalid input format; Value must be an integerin \<210\> in SEQID |
| W | 402 | Undefined organism found in \<213\>  in SEQ ID (0) |
| E | 257 | Invalid sequence data feature in \<221\>  in SEQ ID (0) |
| E | 202 | Invalid input format; Value must be an integerin \<210\> in SEQID |
| W | 402 | Undefined organism found in \<213\>  in SEQ ID (0) |
| E | 257 | Invalid sequence data feature in \<221\>  in SEQ ID (0) |
| E | 202 | Invalid input format; Value must be an integerin \<210\> in SEQID |
| W | 402 | Undefined organism found in \<213\>  in SEQ ID (0) |

Input Set:

Output Set:

|  |  |
|---|---|
| Started: | 2009-04-15 14:29:52.963 |
| Finished: | 2009-04-15 14:30:12.857 |
| Elapsed: | 0 hr(s) 0 min(s) 19 sec(s) 894 ms |
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| No. of SeqIDs Defined: | 259 |
| Actual SeqID Count: | 238 |

| Error code | | Error Description |
|---|---|---|
| E | 257 | Invalid sequence data feature in <221>  in SEQ ID (0) |
| E | 202 | Invalid input format; Value must be an integerin <210> in SEQID |
| W | 402 | Undefined organism found in <213>  in SEQ ID (0) |
| E | 257 | Invalid sequence data feature in <221>  in SEQ ID (0) |
| E | 202 | Invalid input format; Value must be an integerin <210> in SEQID |
| W | 402 | Undefined organism found in <213>  in SEQ ID (0) |
| E | 257 | Invalid sequence data feature in <221>  in SEQ ID (0) |
| E | 202 | Invalid input format; Value must be an integerin <210> in SEQID |
| W | 402 | Undefined organism found in <213>  in SEQ ID (0) |
| E | 257 | Invalid sequence data feature in <221>  in SEQ ID (0) |
| E | 202 | Invalid input format; Value must be an integerin <210> in SEQID |
| W | 402 | Undefined organism found in <213>  in SEQ ID (0) |
| E | 257 | Invalid sequence data feature in <221>  in SEQ ID (0) |
| E | 202 | Invalid input format; Value must be an integerin <210> in SEQID |
| W | 402 | Undefined organism found in <213>  in SEQ ID (0) |
| E | 257 | Invalid sequence data feature in <221>  in SEQ ID (0) |
| E | 202 | Invalid input format; Value must be an integerin <210> in SEQID |
| W | 402 | Undefined organism found in <213>  in SEQ ID (0) |
| E | 257 | Invalid sequence data feature in <221>  in SEQ ID (0) |
| E | 202 | Invalid input format; Value must be an integerin <210> in SEQID |
| W | 402 | Undefined organism found in <213>  in SEQ ID (0) |
| E | 257 | Invalid sequence data feature in <221>  in SEQ ID (0) |

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                    Input Set:


                    Output Set:



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                Finished:   2009-04-15 14:30:12.857
                 Elapsed:   0 hr(s) 0 min(s) 19 sec(s) 894 ms
          Total Warnings:   341
            Total Errors:   2028
    No. of SeqIDs Defined:  259
       Actual SeqID Count:  238


  Error code      Error Description


  E   202         Invalid input format; Value must be an integerin <210> in SEQID

  W   402         Undefined organism found in <213>  in SEQ ID (0)

  E   257         Invalid sequence data feature in <221>  in SEQ ID (0)

  E   202         Invalid input format; Value must be an integerin <210> in SEQID

  W   402         Undefined organism found in <213>  in SEQ ID (0)

  E   257         Invalid sequence data feature in <221>  in SEQ ID (0)

  E   202         Invalid input format; Value must be an integerin <210> in SEQID
                  (0)

  W   402         Undefined organism found in <213>  in SEQ ID (0)
                    This error has occured more than 20 times, will not be displayed

  E   257         Invalid sequence data feature in <221>  in SEQ ID (0)

  E   257         Invalid sequence data feature in <221>  in SEQ ID (0)
                    This error has occured more than 20 times, will not be displayed

  E   253         The number of bases differs from <211>  Input: 20  Calculated:19

  E   259         Found undefined lettercode; POS (22) SEQID(0)

  E   259         Found undefined lettercode; POS (23) SEQID(0)

  E   259         Found undefined lettercode; POS (24) SEQID(0)

  E   259         Found undefined lettercode; POS (25) SEQID(0)

  W   112         Upper case found in data; Found at position(25) SeqId(0)

  W   112         Upper case found in data; Found at position(26) SeqId(0)

  W   112         Upper case found in data; Found at position(27) SeqId(0)

  E   253         The number of bases differs from <211>  Input: 21  Calculated:28

  E   259         Found undefined lettercode; POS (21) SEQID(0)

  E   259         Found undefined lettercode; POS (22) SEQID(0)
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           Input Set:


           Output Set:



               Started:    2009-04-15 14:29:52.963
              Finished:    2009-04-15 14:30:12.857
               Elapsed:    0 hr(s)  0 min(s)  19 sec(s)  894 ms
        Total Warnings:    341
          Total Errors:    2028
  No. of SeqIDs Defined:   259
      Actual SeqID Count:  238


Error code       Error Description


E  259       Found undefined lettercode; POS (23) SEQID(0)

E  259       Found undefined lettercode; POS (24) SEQID(0)

W  112       Upper case found in data; Found at position(24) SeqId(0)

W  112       Upper case found in data; Found at position(25) SeqId(0)

W  112       Upper case found in data; Found at position(26) SeqId(0)

E  253       The number of bases differs from <211>  Input: 20  Calculated:27

E  259       Found undefined lettercode; POS (21) SEQID(0)
              This error has occured more than 20 times, will not be displayed

W  112       Upper case found in data; Found at position(24) SeqId(0)

W  112       Upper case found in data; Found at position(25) SeqId(0)

W  112       Upper case found in data; Found at position(26) SeqId(0)

E  253       The number of bases differs from <211>  Input: 20  Calculated:27

W  112       Upper case found in data; Found at position(24) SeqId(0)

W  112       Upper case found in data; Found at position(25) SeqId(0)

W  112       Upper case found in data; Found at position(26) SeqId(0)

E  253       The number of bases differs from <211>  Input: 20  Calculated:27

W  112       Upper case found in data; Found at position(24) SeqId(0)

W  112       Upper case found in data; Found at position(25) SeqId(0)

W  112       Upper case found in data; Found at position(26) SeqId(0)

E  253       The number of bases differs from <211>  Input: 20  Calculated:27

W  112       Upper case found in data; Found at position(24) SeqId(0)

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W  112       Upper case found in data; Found at position(26) SeqId(0)
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```
                    Input Set:


                    Output Set:



                    Started:   2009-04-15 14:29:52.963
                   Finished:   2009-04-15 14:30:12.857
                    Elapsed:   0 hr(s) 0 min(s) 19 sec(s) 894 ms
          Total Warnings:   341
            Total Errors:   2028
    No. of SeqIDs Defined:   259
        Actual SeqID Count:   238


Error code          Error Description

E   253         The number of bases differs from <211>  Input: 20  Calculated:27

W   112         Upper case found in data; Found at position(27) SeqId(0)

W   112         Upper case found in data; Found at position(28) SeqId(0)
                 This error has occured more than 20 times, will not be displayed

E   253         The number of bases differs from <211>  Input: 23  Calculated:30

E   253         The number of bases differs from <211>  Input: 23  Calculated:30

E   253         The number of bases differs from <211>  Input: 19  Calculated:26

E   253         The number of bases differs from <211>  Input: 23  Calculated:30

E   253         The number of bases differs from <211>  Input: 23  Calculated:30

E   253         The number of bases differs from <211>  Input: 21  Calculated:28

E   253         The number of bases differs from <211>  Input: 21  Calculated:28

E   253         The number of bases differs from <211>  Input: 23  Calculated:30

E   253         The number of bases differs from <211>  Input: 23  Calculated:30

E   253         The number of bases differs from <211>  Input: 21  Calculated:28

E   253         The number of bases differs from <211>  Input: 21  Calculated:28

E   253         The number of bases differs from <211>  Input: 21  Calculated:28
                SEQID (0)

E   252         Calc# of Seq. differs from actual; 259 seqIds defined; count=238

E   250         Structural Validation Error; Sequence listing may not be indexable
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SEQUENCE LISTING

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<212> DNA
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| APPLICATION NO. /CONTROL NO. | FILING DATE | FIRST NAMED INVENTOR / PATENT IN REEXAMINATION | ATTORNEY DOCKET NO. |
|---|---|---|---|
| 10542937 | 9/8/2006 | MATA LOPEZ ET AL. | U 015859-4 |

| EXAMINER |
|---|
| STEPHEN KAPUSHOC |

| ART UNIT | PAPER |
|---|---|
| 1634 | 20090622 |

DATE MAILED:

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents**

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) before the application can be examined under 35 U.S.C. §§ 131 and 132.

APPLICANT IS GIVEN ONE MONTH FROM THE DATE OF THIS LETTER WITHIN WHICH TO COMPLY WITH THE SEQUENCE RULES, 37 C.F.R.. §§ 1.821-1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 C.F.R. § 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 C.F.R. § 1.136. In no case may an applicant extend the period for response beyond the six month statutory period. Direct the response to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the response.

The addresses below are effective 5 June 2004. Please direct all replies to the United States Patent and Trademark Office via one (1) of the following:

1.  Electronically submitted through EFS-Web (<http://www.uspto.gov/ebc/efs/downloads/documents.htm>, EFS Submission User Manual - ePAVE)
2.  Mailed to:
    Mail Stop Sequence
    Commissioner for Patents
    P.O. Box 22313 1450
    Alexandria, VA 22313 1450
3.  Hand Carry, Federal Express, United Parcel Service or other delivery service to:
    U.S. Patent and Trademark Office
    Mail Stop Sequence
    Customer Window
    Randolph Building
    401 Dulaney Street
    Alexandria, VA 22314

Any inquiry concerning this communication should be directed to Stephen Kapushoc at telephone number (571)272-3312. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz, can be reached on (571)272-0763.

/Stephen Kapushoc/
Examiner, Art Unit 1634

PTO-90C (Rev.3-98)

| Notice to Comply | Application No. *** | Applicant(s) *** |
|---|---|---|
| | Examiner *** | Art Unit *** | |

## NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☒ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: Please see the Sequence Listing Reviewer's comments on the included CRFD and Validation report.

### Applicant Must Provide:
☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", **as well as an amendment specifically directing its entry into the application**.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216 or (703) 308-2923
For CRF Submission Help, call (703) 308-4212 or 308-2923
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